REMARKS

Claims 15-31, 43-45 and 47-51 are pending. Claims 1-14, 32-42 and 46 have been canceled without prejudice. Claim 15 has been amended and claims 52 and 53 added.

Claims 15-19, 21, 23-31 and 44 and 47-51 were rejected under 35 USC 103 as being unpatentable over Nelson et al in view of Carninci et al. This rejection is essentially the same as previously.

From the rejection mailed May 26, 2004, it appears the examiner has not appreciated the claim language in its fullness and the processes used by the references. Applicants apparently have not made it clear that the claimed method contains steps not disclosed nor suggested by either reference. Step (d) states that the "sub-group" is a "sub-group of said one or more groups of members of said non-normalized cDNA library represented in high amounts by said RNA sample". As indicated in step (e) this sub-group may then be used to identify and subtract themselves from the group of cDNAs obtained in high amounts by the original RNA sample. Neither reference performs these steps nor suggests doing so.

Nelson et al divides their high abundance cDNAs into differing levels of abundance. The examiner has contended that this separates the group into "subgroups". However, Nelson et al merely identified these "subgroups", Nelson et al do not do any further step with the "subgroups". Nelson et al does not provide any motivation to use these "subgroups" for any particular purpose in an overall process of creating a library.

Carninci et al never even forms a "subgroup". The examiner has pointed to the "minilibraries" in Carninci et al but these are quite different from the claimed "sub-group". Carninci et al's minilibrary is a cDNA library obtained from a different RNA originating from a different tissue. See the second paragraph under "Reduction of the Frequency of Highly Expressed cDNAs". By contrast, the claimed sub-group is a "sub-group of said one or more groups of members of said non-normalized cDNA library represented in high amounts by said RNA sample".

Carninci et al use their minilibraries in a different way, for a different purpose and to produce a different result. Carninci et al uses minilibraries to subtract cDNAs from the high abundance group to discard them and does so to find rare new cDNAs. By contrast, applicants use sub-groups to bring all members of that sub-group cDNAs together to keep them together so that they may be sequenced and identified as belonging to that sub-group. Rare cDNAs do not even exist in the claimed group, as the claimed group by definition constitutes those "represented in high amounts by said RNA sample".

As a separate issue, claim 15 step (f) recites forming a second sub-group, which are a part of "said non-normalized cDNA library represented in high amounts by said RNA sample" but not part of the first sub-group. Nelson et al may identify additional "subgroups" but it is by a method different from that claimed in step (e) and (f). Again Nelson et al does nothing further with their "subgroups" in any type of process of forming a cDNA library. Carninci et al use their "second" minilibrary simultaneously, not separately. Also because each Carninci et al minilibrary is from a different RNA source, the second minilibrary/"subgroup" cannot be from the same source as the first minilibrary/"subgroup" as required by the present claims. Further, unlike the present invention, in Carninci et al any second (or more) minilibrary is not modified or determined by a first (or earlier) minilibrary.

Regarding claim 30, neither reference makes or uses a probe from a sub-group of the original group of cDNAs from high abundance RNA.

Still further, there is nothing in either reference suggesting the "round-robin" type or repetition to form distinct subgroups as recited in step (f). This is expanded in claim 43 where the repeated process to obtain a complete set of subgroups is further highlighted.

The arguments presented in the previous response filed January 26, 2004 also apply. Particularly note that dividing a group into subgroups to retain them for further steps, such as sequencing, is different from subtracting and discarding most members from a group to identify rare members. Accordingly, the rejection should be withdrawn.

Claims 48-51 emphasized the use of plural samples as RNA sources to generate the library. The examiner contends that the prior art, each using only one sample source of

RNA, is somehow considered to disclose plural RNA sources because the initial sample is a mixture. This alleged inherency misses the point that applicants preferred embodiment uses a pool of RNA from many distinct and radically different sample sources. Should the examiner still not see the difference, new claims 52 and 53 recite such a pool of sample sources that even her misinterpretation cannot suggest these claims.

Claim 20 was rejected under 35 USC 103 as being unpatentable over Nelson et al in view of Carninci et al and further in view of Somerville et al. The reasons why the basic rejection is overcome are given above. Somerville et al adds nothing as to the normalization and handling of subgroups of cDNAs. Therefore, this dependant claim should stand with its independent claim and the rejection withdrawn.

Claim 22 was rejected under 35 USC 103 as being unpatentable over Nelson et al in view of Carninci et al and further in view of El-Meanawy et al. The reasons why the basic rejection is overcome are given above. El-Meanawy et al adds nothing as to the normalization and handling of subgroups of cDNAs. Therefore, this dependant claim should stand with its independent claim and the rejection withdrawn.

Claims 51 were rejected under 35 USC 103 as being unpatentable over Nelson et al in view of Carninci et al in further view of Xu et al. Xu et al adds no further teachings to the process for producing a cDNA library using the claimed normalization and handling of subgroups of cDNAs. Therefore, this dependant claim should stand with its independent claim and the rejection withdrawn for reasons above.

CONCLUSIONS

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. Should any further issues remain or the examiner wish

clarification on the rather complex nature of the invention, the examiner is encouraged to contact the undersigned below.

The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No. 500933.

Respectfully submitted,

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